Remarks on Amendment

Upon entry of the foregoing amendment, claims 1-7 are pending in the application, with claim 1 being the independent claim. Claims 1 and 2 have been amended. Support for the amendment for claims 1 and 2 can be found at least at page 4, line 14. These changes are believed to introduce no new matter, and their entry is respectfully requested.

In the Office Action dated July 15, 2003, the claims were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicant filed a reply on October 15, 2003, addressing the enablement rejection. Applicant submitted Hickman *et al.*, *J. Immunol. 171*:22-26 (2003) and Herbert *et al.*, *Human Immunol. 64*:44-55 (2003) in support of Applicant's argument.

In the Advisory Action issued on December 3, 2003, the Examiner stated that

> the references submitted by the Applicant in support of their argument actually demonstrate the unpredictability and the lack of understanding in the art surrounding the Applicant's invention. . . From these refernece [sic] it is apparent that one skilled in the art would not know how to make or use vaccines based upon the identification of upregulated proteins by the Applicant's method because they would not know whether such proteins are effective for inducing a protective or a pathogenic response.

Advisory Action, p. 2.

Applicant submits herewith a Declaration Under 37 C.F.R. § 1.132 of Dr. Donald F. Hunt ("the Hunt Declaration"). The Hunt Declaration states that Hickman *et al.* and Herberts *et al.* (along with at least two other articles, Veronese *et al.*, *J. Exp. Med 183*:2509-2516 (1996) and Overwijk *et al.*, *Proc. Natl. Acad. Sci USA 96*:2982-2987 (1999)) confirm the plausibility of potential vaccine targets for infectious diseases which are based on differentially expressed self-peptides.

As stated in the Hunt Declaration, vaccines have traditionally focused on inducing an immune response against the peptides or proteins of the infectious agent itself. Hickman *et al.*, Herberts *et al.*, and Veronese *et al.* confirm the presence (or at least the plausibility) of an immune response against peptides which are overexpressed during infection. Vaccination with self-antigens has been shown to be effective in treating and preventing cancer, as shown in Overwijk *et al.*, despite the presence of autoimmune responses, such as vitiligo.

Additionally, peptides which are overexpressed by a factor of 9 or greater, as recited in the present claims, or only expressed during infection, are less likely to induce a pathogenic response than peptides which are only slightly overexpressed during infection. One of ordinary skill in the art would only expect a pathogenic immune response against peptides which are prevalent in non-infected cells.

Thus, Applicant believes that the present claims are fully enabled, and meet all the requirements of 35 U.S.C. § 112, first paragraph.

Prompt and favorable consideration of this Preliminary Amendment is respectfully requested. Applicant believes the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Andrea Jo Kamage

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Agent for Applicant
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Date: May 17, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 3613
Zauderer	Art Unit: 1648
Appl. No. 09/966,746	Examiner: Lucas, Z.
Filed: October 1, 2001	Atty. Docket: 1821.0060001
For: **Method of Screening for Therapeutics for Infectious Diseases**	

Declaration Under 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, the undersigned, Dr. Donald F. Hunt, residing at 970 Old Ballard Road, Charlottesville, Virginia 22901, declare and state as follows:

1. I am University Professor of Chemistry and Pathology at the University of Virginia. My research contributions have been recognized by various awards, including the Distinguished Contribution Award, American Society of Mass Spectrometry, 1994; University of Virginia, Inventor of the Year Award, 1995; Christian B. Anfinsen Award, Protein Society, 1996; Chemical Instrumentation Award, American Chemical Society, 1997; Field and Franklin Award, American Chemical Society, 2000; and the Thomson Medal, International Mass Spectrometry Society, 2000.

2. A current curriculum vitae is appended hereto.

3. Based on my education and experience, I am an expert in peptide immunology and mass spectrometry.

4. I am familiar with the above-identified patent application ("patent application") including the claims, the Advisory Action dated December 3, 2003; Veronese *et al.*, *J. Exp. Med. 183*:2509-2516 (1996); Hickman *et al.*, *Immunol. 171*:22-26 (2003); and Herberts *et al.*, *Human Immunol. 64*:44-55 (2003).

5. The invention claimed in the patent application relates to the field of immunology of infectious diseases. More particularly, the invention relates to the art or field of vaccine development for infectious diseases. In my opinion, a person of ordinary skill in the art of immunology of infectious diseases would have a Ph.D. degree in a field related to immunology, microbiology or virology.

6. The Advisory Action states that one of skill in art would not know how to make or use vaccines based upon the application. In my opinion, one of ordinary skill in the art would be able to use the claimed invention, and would expect to find potential vaccine targets using the invention. Detailed support for my opinion is set forth below.

7. The claimed invention is directed to a method of identifying potential vaccine targets by screening for the immunogenicity of self-peptides that are either expressed only during infection or that are overexpressed by a factor of 9 or more during infection.

8. The patent application discloses several methods of identifying self peptides that are differentially expressed during infection, and several methods of determining whether or not those self-peptides can induce an immune response.

9. The object of a vaccine for an infectious disease is to induce an immune response which is specific for the disease state. Immune responses include cellular (CD8 and CD4 T cell responses) and humoral (antibodies). Traditionally, vaccines focus on inducing an immune response against the proteins or peptides of the infectious agent itself. The claimed invention differs in that it seeks to identify vaccine candidates which would be used to induce an immune response against the proteins or peptides of the host cell.

10. Hickman *et al.* identified several class I MHC-presented peptides derived from host proteins overexpressed during HIV infection. This fact is important, because in order to provoke a cellular immune response, peptides must be presented in the context of MHC proteins.

11. Herberts *et al.* identified peptides which are derived from two self-proteins which are upregulated following measles virus infection. These peptides are presented in the context of MHC proteins. Herberts *et al.* also identify CD8 T cells which recognize these self-peptides. These CD8 T cells are functionally activated during natural measles virus infection.

12. Veronese *et al.* describe the presence, in HIV-infected patients, of CD8 T cells specific for self-peptides which are overexpressed during HIV infection.

13. It is my opinion that, based on the specification and general knowledge of the art, a person of ordinary skill in the art would be able to use the methods of the present invention to identify potential vaccine targets. The plausibility of potential vaccine targets which are based on differentially expressed self-peptides is confirmed by Hickman *et al.*, which shows that overexpressed self-peptides may be presented in an MHC context; and Herberts *et al.*, and Veronese *et al.*, which both show an actual immune response against self-peptides overexpressed during infection.

14. Identification and use of vaccine targets which are self-peptides is prevalent in the field of tumor immunology. Several methods of vaccination using self-antigens are well known and studied, including vaccination with the peptides themselves, vaccination

with polynucleotide vectors encoding the peptides, and treatment with autologous cells which have been exposed to the peptide.

15. Vaccination with self-antigens has been shown effective in treating and preventing cancer. For example, Overwijk *et al.*, *Proc. Natl. Acad. Sci USA 96*:2982-2987 (1999) describes the immunization of mice with viral vectors encoding five different self-antigens which are overexpressed in melanoma. Overwijk *et al.* showed that vaccination with one of these viral vectors resulted in tumor protection in all mice studied.

16. Given that tumor vaccines based on overexpressed self-peptides have been shown to be effective, and immune responses have been shown against self-peptides in infectious diseases, it is my opinion that one of ordinary skill in the art would expect to find potential vaccine targets for infectious diseases using the methods of the present invention. One of ordinary skill would also know how to actually make and test vaccines based on targets found through the claimed method.

17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the present patent application or any patent issued thereon.

Respectfully submitted,

Donald F Hunt

Dr. Donald F. Hunt

Date: 4/28/04